Remarks

The Amendments

The specification has been amended to remove all embedded hyperlinks. Each hyperlink has been replaced with a written description of the Uniform Resource Locator, or web address, that accesses each hyperlink. For instance, "http://www.gen.emory.edu/mitomap.html " has been amended to "the website having the URL address: http file type, www host server, gen.emory.edu domain name, mitomap.html directory."

None of these amendments introduce new matter.

The Rejection of Claims 1-11 and 29-53 Under 35 U.S.C. § 112, First Paragraph

Claims 1-11 and 29-53 have been rejected under 35 U.S.C. § 112, first paragraph as not adequately described. Applicants respectfully traverse.

To comply with the written description requirement, the description must clearly convey to persons of ordinary skill in the art that applicants invented what is claimed. *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989). The Patent Office has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *In re Wertheim*, 541 F.2d 257 (CCPA 1976). See also MPEP § 2163.04. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. *The Regents of the University of California v. Eli Lilly and Company*, 119 F.3d 1559 (Fed. Cir. 1997). A representative number is an inverse function of the skill and knowledge in the art. The number of

species that must be disclosed to satisfy disclosure of a representative number of species depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. MPEP § 2163(II)(A)(3)(a)(ii). Written description of a representative number of species does not require the disclosure to be of such specificity that it would provide individual support for each species that the genus embraces. MPEP § 2163(II)(A)(3)(a)(ii).

Claims 1 and 35 are the independent claims of the rejected claim set. Each of these claims is directed to a method to aid in detecting the presence of tumor cells in a patient. Claim 1 recites "that the presence of a homoplasmic single basepair substitution" is determined in a mitochondrial genome of a cell sample of a patient. The "substitution is found in a tumor of the patient but not in normal tissue of the patient." The patient is identified "as having a tumor if one or more single basepair substitutions are determined in the mitochondrial genome of the cell sample of the patient." Claim 35 differs from claim 1 in additionally reciting that "the mutation has previously been identified as a somatic mutation in a tumor" and in not reciting that the mutation is a homoplasmic single basepair substitution.

The Office Action asserts that these claims are not adequately described because the specification does not disclose a sufficient number of mitochondrial mutations that can be used to identify a patient as having a tumor.

> The specification at page 1 discloses that the human mitochondrial genome is a large, 16 kilobase circular double-stranded DNA. The specification further teaches in example 1 (pages 9-11) and Table 1 (page 17), the identification of 12 somatic mutations of the human mitochondrial DNA of human colorectal cancer cells. The

> specification however fails to describe or disclose a representative number of single basepair mutations of the human mitochondrial DNA encompassed by the instant claims as written. The instant claims as written encompasses a plethora of single basepair mutations not disclosed or described anywhere in the specification. Additionally, it cannot be determined if any basepair mutation, besides those mentioned in Table 1, is capable of functioning in the method of determining the presence and absence of a tumor in a patient.

Paper 7, page 5, lines 6-15. The Patent Office has failed to meet its burden of presenting a preponderance of evidence why a person skilled in the art would not recognize from the disclosure that applicants invented what is claimed. The Patent Office has baldly asserted that mutations other than those specifically disclosed may not be functional in the claimed methods. No evidence or sound scientific reasoning supports this assertion.

First, the Patent Office implies that because the mitochondrial genome contains approximately 16×10^3 basepairs the specification's disclosure of twelve mitochondrial DNA (mtDNA) mutations cannot adequately describe the genus of homoplasmic single basepair substitutions or single basepair mutations. However, because the twelve disclosed mutations occur at positions dispersed throughout the mitochondrial genome and in regions that code for proteins as well as in regions that do not code for proteins they are representative of mutations anywhere in the mitochondrial genome. The disclosed twelve mutations are located at nucleotide positions 710, 1738, 1976, 2299, 3308, 6264, 8009, 9949, 10563, 12418, 14985, and 15572 in the mitochondrial genome. See Table 1 at page 17 of the specification. Eight of the twelve somatic mutations are in protein encoding genes and four are in rRNA encoding genes, *i.e.*, non-protein coding regions. See specification at page 11, lines 5-6. Thus the twelve mtDNA mutations are

representative of the genus of single base pair mtDNA mutations in their genetic dispersion and in their functionality.

Second, the Patent Office speculates that if a mtDNA mutation, other than the twelve disclosed in the specification, is detected in a cell sample it might not be a mutation that can identify a patient as having a tumor. Claim 1 recites that the mutation is a "homoplasmic single basepair substitution." One of skill in the art would expect that to be so based on the homoplasmy. Applicants have taught that such a mutation would identify a patient as having a tumor, whether or not it is disclosed in Table 1. Claim 35 recites that the mutation "has previously been identified as a somatic mutation in a tumor." Clearly such a mutation that has previously been associated with a tumor would identify a patient as having a tumor, whether or not it is disclosed in Table 1. The Patent Office has provided no reasons or evidence to rebut applicant's presumptively correct teachings. Having failed to provide any evidence the Patent Office has not met its burden in presenting a *prima facie* case.

Withdrawal of this rejection to claims 1-11 and 29-53 is respectfully requested.

The Rejection of Claims 1-11 and 29-53 for Obviousness-Type Double Patenting

Claims 1-11 and 29-53 have been rejected for obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 6,344,322. A terminal disclaimer will be filed upon receiving notification that the claims are otherwise in condition for allowance. Applicants respectfully request that the rejection be held in abeyance.

Respectfully submitted,

Date: June 30, 2003

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